REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks and that all of the claims remaining be allowed.

Claim Amendments

Claims 21-24 have been amended to recite "a human IL-B50 receptor" instead of "IL-B50 receptor". Support for this amendment can be found, for example, at page 12, lines 14-15.

Claims 23 and 24 have also been amended to recite a 90% sequence identity, for which support can be found, for example, at page 15, line 29 to page 16, line 2.

No new matter has been added by these amendments. The Examiner is hereby requested to enter these amendments.

Applicants submit that all claim amendments presented herein or previously are made solely in the interest of expediting allowance of the claims and should not be interpreted as acquiescence to any rejections or ground of unpatentability. Applicants reserve the right to file at least one continuing application to pursue any subject matter that is canceled or removed from prosecution due to the amendments.

Rejections Under 35 U.S.C. §112, Written Description (Paragraphs 5 and 7 of the Office Action)

The rejection of claims 22-24 and 30-32 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, is respectfully traversed for the reasons set forth below.

Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of

drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, Paragraph 1, "Written Description" Requirement, Federal Register 66(4):1099, 1104 (2001). Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. Examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. *Id.* at 1110 (Footnote 42).

Claim 22 is directed to a purified polypeptide wherein the polypeptide comprises SEQ ID NO: 4, or a fragment thereof, capable of binding a human IL-B50 receptor. Claim 23, as amended, is directed to a purified polypeptide comprising an amino acid sequence that is at least about 90% identical to the amino acid sequence of SEQ ID NO: 2, or a fragment thereof, wherein the polypeptide is capable of binding a human IL-B50 receptor. Similarly, all other claims at issue relate to polypeptides that are similar in sequence to SEQ ID NO:2 or SEQ ID NO:4, wherein the polypeptides bind a human IL-B50 receptor.

As discussed in Applicants' last response, filed May 25, 2004, the present specification describes distinguishing identifying characteristics sufficient to show that Applicants were in possession of the claimed invention. Briefly, the specification provides the IL-B50 sequences SEQ ID NO:2 and SEQ ID NO:4. The specification further describes the structural motifs in the disclosed sequences, including those important for receptor binding. It is disclosed that the IL-B50 sequence has a signal peptide at the N terminus, which is about 33 residues long (page 10, lines 23-25). IL-B50 exhibits structural motifs characteristic of a member of the short chain cytokines, which are known to have four alpha helices. The locations of the four helices, A-D, are shown in Figures 1A and 1B. It is further disclosed that helices A and D are the most important in receptor interaction (page 40, lines 21-22). Surface exposed residues would affect receptor binding (page 40, lines 25-26). Sequence variants preferably have substitutions away

from the conserved cysteines, and often will be in the regions away from the helical structural domains (page 17, lines 7-10).

The Office Action ignores the claim element "capable of binding IL-B50 receptors", stating (page 3):

> the claims only require the polypeptide to be capable of binding a putative IL-B50 receptor, function and biological significance of which at the time of invention appears to be not disclosed. Thus, one would reasonably conclude that the claims are drawn to a genus of polypeptides that is defined only by sequence identity.

Applicants disagree. The present application discloses that the human IL-B50 receptor consists of two subunits, hIL-7Rα and hRδ2 (page 64, lines 10-12). When Ba/F3 cells were co-transfected with both hIL-7Rα and hRδ2, the transfectants proliferated in response to IL-B50 but not IL-7 (page 64, lines 6-7). Ba/F3 cells transfected with either hIL-7Rα or hRδ2 alone did not respond to IL-B50 (page 64, lines 7-9). Expression patterns of the receptor subunits are also disclosed (page 64, lines 17-27 and Figure 2). Thus, the specification discloses the structure and function of the IL-B50 receptor by actual reduction to practice. Therefore, the IL-B50 receptor is well described in the present application.

The IL-B50 receptor is also well described in the priority applications of the present application. For example, U.S. Provisional Application No. 60/101,318 ("the '318 application"), filed September 21, 1998, discloses that IL-B50 is a cytokine which functions via a receptor (see, e.g., page 9, lines 2-9). As taught in the '318 application and well known in the art, when a ligand of a specific ligand-receptor interaction has been isolated, a person of ordinary skill can readily isolate its receptor (page 49, lines 5-25). Thus a ligand defines its specific receptor, and the identity of the ligand serves as a sufficiently distinguishing identifying characteristic for its receptor. Since the '318 application discloses the sequence of the IL-B50 ligand, it provides adequate description of the IL-B50 receptor. Furthermore, the '318 application also describes the IL-B50 receptor as having an alpha and a beta subunit, and the beta subunit of the IL-B50 receptor should be the alpha subunit of the IL-7 receptor (page 49, lines 25-35). Taken together, the '318 application provides both the ligand binding specificity and partial structure of the

IL-B50 receptor, thus one skilled in the relevant art would agree that the inventors had possession of the IL-B50 receptor on the filing date of the '318 application.

In view of the above, the IL-B50 receptor is adequately described. In contrast to the assertion in the Office Action, the claimed polypeptides are not "defined only by sequence identity", but are also defined by functional characteristics, in this case binding activity to the IL-B50 receptor. Since the specification discloses SEQ ID NO:2, SEQ ID NO:4, sequence motifs important for receptor binding, as well as the IL-B50 receptor, identifying characteristics sufficient to distinguish the claimed polypeptides are provided. Therefore, the written description requirement is satisfied.

Rejections Under 35 U.S.C. §112, Enablement (Paragraph 6 of the Office Action)

The rejection of claims 22-24 and 30-32 under 35 U.S.C. §112, first paragraph, as allegedly not being enabled, is respectfully traversed for the reasons set forth below.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. MPEP §2164.01; *United States v. Telectronics, Inc.*, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). As pointed out in the Office Action, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 8 USPQ2d 1401 (Fed. Cir. 1988). These factors are discussed below in an order that is convenient for discussion.

Nature of the invention and breadth of claims

The claimed invention relates to specific polypeptides and polypeptide compositions. Specifically, claim 22 is directed to a purified polypeptide wherein the polypeptide comprises SEQ ID NO: 4, or a fragment thereof, capable of binding a human IL-B50 receptor. Claim 23, as

amended, is directed to a purified polypeptide comprising an amino acid sequence that is at least about 90% identical to the amino acid sequence of SEQ ID NO: 2, or a fragment thereof, wherein the polypeptide is capable of binding a human IL-B50 receptor. Similarly, claim 24 is directed to a purified polypeptide comprising an amino acid sequence that is at least 90% identical to amino acids 1 through 131 of SEQ ID NO: 4, or a fragment thereof, wherein the polypeptide is capable of binding a human IL-B50 receptor. Claims 30 and 31 are directed to fusion proteins comprising the polypeptide of claim 22 or 23. Claim 32 is directed to a composition comprising the polypeptide of any of claims 22-24.

State of the art, predictability, and relative skill in the art

The present application was filed on September 25, 2001, with a priority date of September 21, 1998. At the time the priority application was filed, recombinant DNA techniques and peptide synthesis had already become routine practice in the relevant field. The references cited in the present application (page 19, lines 21-30) are just a few examples demonstrating the state of the art. Given this state of the art, if the sequence of a polypeptide was known, it was well within the state of the art to prepare fragments or variants, such as variants having a 90% sequence identity, of the polypeptide. Similarly, methods of isolating a specific receptor for a known ligand, as well as binding assays between a ligand and its receptor, are also well known in the art. Furthermore, the structure and functions of short chain cytokines are well known. Accordingly, the level of predictability in the relevant art is relatively high.

As pointed out in the Office Action, the relative skill in the relevant art is high.

Amount of direction or guidance presented and working examples

The specification provides ample guidance for the claimed invention. The working examples provide SEQ ID NO:2 and SEQ ID NO:4. Methods of preparing variants (see, e.g., pages 15-18) and isolating receptor (see, e.g., pages 45-46) are described in detail. As discussed above, structural motifs within the sequences, and regions important for receptor binding, are also disclosed.

Quantity of experimentation necessary

To practice the claimed invention, a practitioner would prepare variants of IL-B50 based on the sequence information of SEQ ID NO:2 and SEQ ID NO:4, and test the activity of these variants to bind the IL-B50 receptor. The quantity of experimentation is not high since the claims require a high degree of sequence identity (at least 90%) with known sequences, or fragments thereof. Furthermore, as discussed below, the quantity of experimentation is not undue in view of the amount of disclosure and knowledge in the art.

No undue experimentation required

A considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 8 USPQ 2d 1401, 1404 (Fed. Cir. 1988). In *Wands*, the claimed invention related to monoclonal antibodies, and hundreds of clones had to be made and tested for binding activity. The Federal Circuit held that no undue experimentation was required, because the specification discloses the methods of making and testing the clones. Similarly, here, a number of variant clones are to be made and their binding activities tested. However, given the state of the art and level of skill in the art, this kind of experimentation was routine at the time the priority application was filed. Since the specification provides methods of making the clones and important regions in the sequences that should not be varied, there is plenty of guidance with respect to the direction in which the experimentation should proceed. Therefore, undue experimentation is not required under *Wands*.

Accordingly, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. §112, Second Paragraph (Paragraph 7 of the Office Action)

The rejection of claims 21-24 and 30-32 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite, has been obviated for the reasons set forth below.

The Office Action states, essentially, that the metes and bounds of "IL-B50 receptor" are not clear. Specifically, the Office Action states that the instant specification "does not identify that

property or combination of properties which are unique to and, therefore, definitive of a 'IL-B50'" (page 7 of the Office Action).

As amended, the claims at issue now recite "a human IL-B50 receptor", of which the metes and bounds are clear. Pursuant to MPEP §2173.02:

> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
> (A) The content of the particular application disclosure;
> (B) The teachings of the prior art; and
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.
> In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent.

The present application discloses the cytokine IL-B50, sequences and uses thereof. Two related sequences, SEQ ID NO:2 and SEQ ID NO:4, are provided for the human IL-B50 (see, e.g., page 12, lines 14-15). Cytokines are well known in the art, and one of ordinary skill would understand that a human IL-B50 receptor refers to a receptor that binds specifically to a naturally occurring human IL-B50. As discussed above, a ligand defines its specific receptor. Therefore, the metes and bounds of the human IL-B50 receptor are clear to those of ordinary skill in the art.

Accordingly, withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. §102 (Paragraph 8 of the Office Action)

The rejection of claims 21-24 and 30-32 under 35 U.S.C. §102(e) in view of Sims et al. (U.S. Patent No. 6,555,520, "the Sims patent") is respectfully traversed for the reasons set forth below.

The Office Action denies the priority dates of the present application, alleging lack of patentable utility disclosure in the priority applications, and deems the Sims patent as prior art for the present application. As discussed in the response filed May 25, 2004, the '318 application discloses at least one utility that is specific, substantial and credible, and the disclosed utility is supported by the data presented in the instant specification. In particular, the '318 application asserts that IL-B50 shares similar biological functions with IL-7 (page 12, second paragraph, particularly line 32), and that IL-7 exhibits strong effects on lymphopoietic development and differentiation (page 59, lines 21-22). Therefore, a skilled artisan would understand that the '318 application discloses a utility of IL-50 as stimulating lymphopoietic development and differentiation. Consistent with the structural and functional similarities, the '318 application also discloses that IL-B50 and IL-7 are so closely related that their receptors would share a common subunit, IL-7α (page 49, lines 25-28). Indeed, the present application discloses that IL-B50 enhances maturation of dendritic cells (page 67) and expansion/ development of T cells (page 68). The IL-B50 receptor has been identified, and it does contain the alpha subunit of the IL-7 receptor (pages 63-64 of the present application). Therefore, the specific and substantial utilities disclosed in the '318 application are also credible.

Even absent the explicit assertion of utility in the '318 application, one of ordinary skill would have imputed the utilities of IL-7 to IL-B50 based on disclosure of the '318 application. Pursuant to the Utility Examination Guidelines, Federal Register 66(4):1092 (2001) (hereinafter "the Utility Guidelines"), when a class of proteins is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein. *Id.* at 1096 (comment 19). Here, the class of IL-7 (such as IL-7 from different species) is known to have specific, substantial, and credible utilities. Given the structural similarity between IL-7 and IL-B50, as well as the disclosure that their receptors share a common subunit, a skilled artisan would have assigned IL-B50 to the IL-7 class upon reading the disclosure of the '318 application. Therefore, the utilities of IL-7 can be reasonably imputed to IL-B50.

In view of the above, the claimed invention is entitled to the benefit of the filing date of the '318 application, namely September 21, 1998. Since the Sims patent was filed on May 9, 2001, with an earliest possible priority date of November 13, 1998, it is not prior art with respect to the claimed invention. Therefore, withdrawal of this rejection is respectfully requested.

Conclusions

For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's objections and rejections are hereby requested. Allowance of the claims remaining in this application is earnestly solicited.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at (650) 839-5044.

Enclosed is a $110.00 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: Dec. 2, 2004

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